

**UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY**

IN RE VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	MDL No. 2875 HON. ROBERT B. KUGLER CIVIL NO. 19-2875 (RBK)
THIS DOCUMENT RELATES TO ALL CASES	

**PLAINTIFFS' BRIEF IN OPPOSITION TO ZHP DEFENDANTS' MOTION
TO AMEND OR CORRECT THE COURT'S OPINION ON THE PARTIES'
LIABILITY EXPERTS AND IN SUPPORT OF PLAINTIFFS' CROSS
MOTION TO EXCLUDE DR. AFNAN'S OPINIONS THAT RELY ON DR.
XUE'S EXCLUDED OPINIONS**

TABLE OF CONTENTS

PRELIMINARY STATEMENT1

ARGUMENT2

 I. THE COURT CORRECTLY TREATED EXPERTS
 DIFFERENTLY BASED ON THEIR EXPERTISE,
 METHODOLOGY, AND THE BASIS FOR AND
 NATURE OF THEIR OPINIONS2

 II. THE COURT SHOULD EXCLUDE ALL OF DR. AFNAN’S
 OPINIONS THAT RELY ON DR. XUE’S EXCLUDED OPINIONS...10

CONCLUSION20

TABLE OF AUTHORITIES

Cases

<i>Brazos River Auth. v. GE Ionics, Inc.</i> , 469 F.3d 416 (5th Cir. 2006)	17
<i>Chevron TCI, Inc. v. Capitol House Hotel Manager, LLC</i> , 541 F. Supp. 3d 687 (M.D. La. 2021)	17
<i>Deutsche Shell Tanker Gesellschaft mbH v. Placid Refining Co.</i> , 993 F.2d 466 (5th Cir. 1993)	17
<i>Diamond Offshore Co. v. Survival Sys. Int'l, Inc.</i> , 902 F. Supp. 2d 912 (S.D. Tex. 2012).....	17
<i>Fuesting v. Zimmer, Inc.</i> , 362 F. App'x 560 (7th Cir. 2010)	10,18
<i>Gopalratnam v. Hewlett-Packard Co.</i> , 877 F.3d 771 (7th Cir. 2017)	10,18
<i>In re Paoli Railroad Yard PCB Litig.</i> , 35 F.3d 717 (3d Cir. 1994)	10,18
<i>Sims v. Kia Motors of Am., Inc.</i> , 839 F. 3d 393 (5th Cir. 2016)	10
<i>In re TMI Litig.</i> , 193 F.3d 613 (3d Cir, 1999)	10,18

PRELIMINARY STATEMENT

The ZHP Defendants' motion to limit the Court's exclusion of some of Dr. Afnan's opinions based on the Court's decisions allowing other experts to opine on the same areas is built on a false premise, as if every other expert has the same expertise, applied the same methodology, and relied on the same basis for and nature of their opinions as Dr. Afnan. Moreover, the ZHP Defendants present Dr. Afnan as their primary counterpart to Dr. Najafi and Dr. Plunkett, when he actually matches up most closely with Plaintiffs' expert Dr. Bain.

Defendants proffer a fanciful legal rule that the exclusion of one party's expert on an issue requires the exclusion of the other party's corresponding expert. If that were true, then the extensive limitations placed on Dr. Bain would apply to Dr. Afnan as well. Of course, that is not the rule, since the Court evaluates each expert individually based on that expert's qualifications, methodology, and the basis for and nature of each opinion.

However, in filing this motion the Defendants unwittingly invited Plaintiffs to cross-move regarding an important basis to exclude a great deal more of Dr. Afnan's proffered opinions, that was not addressed by the Court—likely due to the large volume of *Daubert* motions filed by the Parties.¹ Specifically, Dr. Afnan relied

¹ Plaintiffs intended to address this issue on a motion in limine to preclude experts from offering opinions that are based on other experts' since precluded opinions, which the defense has agreed to in principle; however, in light of the filing of

entirely on Dr. Xue's chemistry and other excluded opinions as the basis for most of his opinions, including that the ZHP Defendants complied with cGMPs and their other regulatory obligations. An important consequence of the Court's exclusion of Dr. Xue's opinions is the evisceration of the basis for Dr. Afnan's opinions. Without that foundational basis, which Dr. Afnan explicitly relied on for his opinions, he has no support for his cGMP and regulatory opinions and other opinions addressed herein regarding the ZHP Defendants. The Court should consequently exclude those opinions.

ARGUMENT

I.

THE COURT CORRECTLY TREATED EXPERTS DIFFERENTLY BASED ON THEIR EXPERTISE, METHODOLOGY, AND THE BASIS FOR AND NATURE OF THEIR OPINIONS

The relief sought by the ZHP Defendants' motion is somewhat unclear until the second to last page, where they ask the Court to "deny plaintiffs' motion to exclude Dr. Afnan in full." (Defs.' Br. 10). The ask seems to be disconnected with the Court's decision excluding parts of Dr. Afnan's report:

In ¶24 of his report, that the VCDs were not adulterated because the way he asserts this opinion is not based on an FDA's or other legal body's determination;

Defendants' motion, Plaintiffs deemed it most efficient to cross-move on this issue related to Dr. Afnan now.

In ¶53, that the lack of standards or guidance in any industry-recognized standard such as an FDA guidance, USP standard, etc. for testing nitrosamines provides LEGAL assurance that ZHP was diligent in testing for nitrosamines; and that the specific guidance document in this paragraph does not provide legally enforceable requirements for pharmaceutical product manufacturers;

¶64, because it is pure ipse dixit;

¶69, any assertion of therapeutical equivalence between VCDs and the RLD, Diovan®;

¶138, as this paragraph states Dr. Afnan's opinions about the definitions of "adulterated" and "bioequivalent", which Afnan is not qualified to state and is therefore not helpful to the fact-finder.

¶153, because Afnan is not a legal expert who may opine on the meaning and implications of the causation opinion of 6 Dec 2022 in *In re Zantac* MDL.

([ECF 2581](#), p. 6-7). The Court's reason for excluding each paragraph in no way applies to Dr. Najafi's or Dr. Plunkett's corresponding opinions, to the extent such opinions exist.

Paragraph 24 of Dr. Afnan's report states:

Plaintiffs' experts lack support for the assertion that generic valsartan was adulterated because it was not bioequivalent to the brand-name Reference Listed Drug ("RLD"), Diovan. Whether a pharmaceutical drug or API is adulterated is a determination made by the FDA; a drug cannot be retroactively deemed adulterated for purposes of litigation. Moreover, the presence of trace impurities in a generic drug or drug component does not affect bioequivalence or render a drug adulterated. And in any event, an independent lab [(Valisure)] (whose nitrosamine

testing has been reviewed and confirmed by Dr. Najafi) identified NDMA in Diovan. Thus, even if bioequivalence were affected by trace impurities, Plaintiffs' experts' theories would still be illogical.

(Ex. 1).² The exclusion was proper. Among other things, Dr. Afnan conceded that he did nothing to confirm the reliability of Valisure's testing, which was found by the FDA to be unreliable. (Afnan 3/8/2023 Dep. Tr. 413:22-415:16 (Ex. 2); FDA Letter to Valisure, dated December 5, 2022 (Ex. 3)). Dr. Afnan also admitted that he never tried to match up the blinded sample test results per Dr. Najafi with the valsartan results reported by Valisure—which do not match up. (Afnan 3/8/2023 Dep. Tr. 412:8-413:4). Most important, he could not answer whether, because the approved Diovan process could not create nitrosamines (as even admitted by Dr. Xue (Xue Dep. Tr. 171:6-10 (Ex. 4)), any NDMA contamination of a Diovan batch or part thereof would actually evidence a cGMP violation. (Afnan 3/8/2023 Dep. Tr. 416:24-419:8).

In contrast, Dr. Najafi and Dr. Plunkett built their opinions on a reliable foundation, including Defendants' own testing and testimony to confirm the existence of NDMA and NDEA in their VCDs and on the FDA and Health Canada's testing for the fact that Diovan and Exforge do not have NDMA and NDEA in them. (Dr. Najafi R., p. 5-6 (Ex. 5); Dr. Plunkett R., p. 30, 33, 41 (Ex. 6)). This is why the

² Unless otherwise noted, all exhibits are attached to the Certification of Adam M. Slater filed with this brief.

Court correctly treated Dr. Afnan's opinions differently from Dr. Najafi's and Dr. Plunkett's.

The 53rd paragraph of Dr. Afnan's report states:

The only references to the FDCA and the CFR in the Quality Agreement guidance document are referrals to definitions stated therein. Thus, this guidance document does not provide legally enforceable requirements for pharmaceutical product manufacturers. It is true that ICH Q7 states that "[t]here should be a written and approved contract or formal agreement between a company and its contractors that defines in detail the GMP responsibilities, including the quality measures, of each party." But, as Bain acknowledges, ZHP did have quality agreements with the finished dose manufacturers. (See, e.g., Bain Rep. at 70 (acknowledging ZHP had quality agreements in place with Princeton, Teva and Torrent).) Such quality agreements appropriately detail the responsibilities of the API and drug product manufacture, including with respect to quality measures, consistent with ICH Q7. (See PRINSTON00463676; PRINSTON00469838; ZHP00697574; see, e.g., ZHP02471359; PRINSTON00161064; PRINSTON00372649; PRINSTON00160785; ZHP02030312; ZHP01940772; ZHP00343409; ZHP02601697; ZHP01941907; TEVA-MDL2875-00020279 (Teva 167); TEVA-MDL2875-00020213 (Teva 168); TEVA-MDL2875-00020214 (Teva 169); TEVA-MDL2875-00020212 (Teva 170).)

(Ex. 1). This is a pure legal opinion: "this guidance document does not provide legally enforceable requirements for pharmaceutical product manufacturers,"³ just

³ Dr. Afnan's report on this point is especially confusing because he then testified: "...cGMPs are a list of what-to-dos as stipulated by the Food and Drug Administration. How those are effectively put into practice is done through the procedures of the firm...**the cGMPs are defined, for API manufacturers in Q7 –**

as Dr. Afnan’s discussion of the *Daubert* decision in the *Zantac* MDL. (*Id.*). Dr. Najafi and Dr. Plunkett never opine on whether a guidance document is definitively “legally enforceable.” (Dr. Najafi R. (Ex. 5); Dr. Plunkett R. (Ex. 6)). And the ZHP Defendants have admitted that they were required to comply with the ICH requirements – as a matter of fact, not opinion. (*See, e.g.*, Peng Dong 3/29/2021 Dep Tr. 33:9-34:10, 35:18-24, 37:5-9, 40:9-11, 55:15-18; 56:22-57:2 (Ex. 7)).

Paragraph 64 of Dr. Afnan’s report states:

When determining which reporting mechanism to use, a drug application holder must rely on the information reasonably available at the time.

(Ex. 1). Dr. Afnan did not provide any support or explanation for this dangling one sentence opinion, or explain what was “reasonably available”. The Court properly excluded it as “pure ipse dixit.” ([ECF 2581](#), p. 6).

Dr. Afnan’s 69th paragraph is similarly conclusory:

Since approval of the ANDA in 2015, Princeton’s drug products (40, 80, 160 and 320 mg Valsartan) continue to be considered therapeutically equivalent to the original drug product, namely Diovan.

ICH guidance Q7. For drug product manufacturers, it’s defined in 210 and 211 of the code of federal regulations. Again, those are the what-to-dos and not the how-to-dos....My point is, the GMPs are a set of what-to-dos and not how-to-dos. **Industry needs to follow the how-to-dos and those how-to-dos are based on – for API manufacturers, are based on Q7...**” (Afnan 2/8/2023 Dep. Tr. 29:24-32:5, 35:8-37:13 (emphasis added); *see also id.* at 37:16-40:15).

(Ex. 1). Nowhere in his opinion does Dr. Afnan define therapeutic equivalence or explain how the ZHP Defendants' VCDs meet that definition—which he cannot since therapeutic equivalence requires the same quality and purity as the RLD as well as compliance with current good manufacturing practices. (*Id.*; Hai Wang 3/10/21 Dep. Tr. 82:4-83:22, 84:2-5, 84:19, 84:22-85:10 (Ex. 8); *Orange Book Preface*, <https://www.fda.gov/drugs/development-approval-process-drugs/orange-book-preface> (Ex. 9, p. 4, 6-8)). There is no reliable basis or methodology to support this opinion, which is fundamentally wrong in light of the confirmed and admitted NDMA and NDEA contamination. (PRINSTON00077339-44 (Ex. 10)). On the other hand, both Dr. Najafi and Dr. Plunkett reliably define therapeutic equivalence and explain why Defendants' VCDs fail to meet that definition. (Dr. Najafi R., p. 10, 29 (Ex. 5); Dr. Plunkett R., p. 41 (Ex. 6)). As a result, the Court properly excluded Dr. Afnan's opinion while permitting those of Dr. Najafi and Dr. Plunkett.

The 138th paragraph of Dr. Afnan's report states:

Fourth, Plaintiffs' experts lack support for the assertion that generic valsartan API was adulterated at the time of sale because it was not bioequivalent to the brand-name RLD, Diovan. Whether a pharmaceutical drug is adulterated is a determination made by the FDA; a drug cannot be retroactively deemed adulterated for purposes of litigation. Moreover, the presence of trace impurities in a generic drug or drug component does not affect bioequivalence or render a drug adulterated. And in any event, an independent lab [(Valisure)] (whose nitrosamine testing has been reviewed and confirmed by Dr. Najafi) identified NDMA ***in Diovan***. Thus, even if bioequivalence

were affected by trace impurities, Plaintiffs' experts' theories would still be illogical.

(Ex. 1). This paragraph was properly excluded for the same reasons as Paragraph 24. Aside from the fatal flaws found by the Court, Dr. Afnan sets up a straw man with this opinion that does not "fit" the case, since Plaintiffs are not asserting that lack of bioequivalence is the basis for adulteration. The ZHP Defendants similarly attempt to obscure the issue by imprecisely referring to the "equivalence" opinions as if they are all the same. (Defs.' Br. 2, 6).

It is the lack of therapeutic equivalence, and corresponding cGMP violations and lack of compliance with the compendiums that underly Plaintiffs' claims here. Additionally, as Plaintiffs explained in their original motion, there is no methodology or analysis underlying Dr. Afnan's obviously inaccurate legal opinion that drugs can only be deemed adulterated by the FDA prospectively. Plaintiffs' experts did not approach the issue the same flawed way, instead analyzing the admissible facts of record and applying the statutory definition.

The Court was well within its authority to prevent Dr. Afnan from providing patently inaccurate legal advice to a jury, or talking about the Valisure situation based solely on innuendo and speculation. As discussed below, Dr. Afnan's opinion as to "how those regulations apply to ZHP's conduct" is also hopelessly tethered to Dr. Xue's precluded opinions, and thus falls with those already precluded opinions as well.

The last paragraph the Court excluded was Paragraph 153:

Moreover, a federal judge recently found that the plaintiffs in litigation involving allegations of NDMA in another pharmaceutical drug “fail[ed] to produce admissible primary evidence” that trace amounts of NDMA in pharmaceuticals are capable of causing cancer. *In re Zantac (Ranitidine) Prod. Liab. Litig.*, No. 20-MD-2924, 2022 WL 17480906, at *167 (S.D. Fla. Dec. 6, 2022). Among other things, the court explained that:

None of the Plaintiffs’ experts have provided reliable primary evidence of dose-response relationship for ranitidine. The Plaintiffs’ experts either fail to address dose-response relationship or provide dose-response relationship opinions derived from unreliable methodologies. Furthermore, the Plaintiffs’ experts have not provided reliable opinions regarding what threshold dose of NDMA causes each of the five Designated Cancers, let alone what threshold dose of ranitidine causes cancer. Based upon the totality of the evidence, none of the Plaintiffs’ experts provided reliable primary evidence of a dose-response relationship for ranitidine and the Designated Cancers. The lack of reliable dose-response relationship opinions casts doubt on the reliability of the Plaintiffs’ experts’ general causation methodologies. *Id.* at *158.

(Ex. 1). This is a legal argument masquerading as an expert opinion, on top of the fact that the Zantac case addressed a different drug, different facts, and a different record. Dr. Najafi and Dr. Plunkett do not proffer any remotely similar opinions. (Dr. Najafi R. (Ex. 5); Dr. Plunkett R. (Ex. 6)).

II.

THE COURT SHOULD EXCLUDE ALL OF DR. AFNAN'S OPINIONS THAT RELY ON DR. XUE'S EXCLUDED OPINIONS

Dr. Afnan relies extensively on Dr. Xue's excluded opinions for his own opinions, and the Court has excluded all of Dr. Xue's substantive chemistry opinions and opinions regarding the July 2017 email. This exclusion is broad and all-encompassing, including generally opinions about "the sufficiency of ZHP's conduct," with the only exception being for background. ([ECF 2581](#), p. 17-18). As a result, all of Dr. Afnan's opinions that rely on Dr. Xue's excluded opinions should be precluded, and because this subsumes all of Dr. Afnan's substantive opinions, he should be precluded altogether. *Gopalratnam v. Hewlett-Packard Co.*, 877 F.3d 771, 789 (7th Cir. 2017) ("plaintiffs cannot reasonably admit through [a second expert] what they could not offer through [the excluded one]"); *Sims v. Kia Motors of Am., Inc.*, 839 F. 3d 393, 405 (5th Cir. 2016) ("[T]he district court properly excluded [the second expert's] theory ... because it relied on [the first expert's] inadmissible ... theory"); *Fuesting v. Zimmer, Inc.*, 362 F. App'x 560, 564 (7th Cir. 2010) ("[B]ecause [an expert's] testimony on causation primarily relies on an excluded expert opinion ..., the district court did not err in excluding it."); *more generally In re Paoli Railroad Yard PCB Litig.*, 35 F.3d 717, 742 (3d Cir. 1994) (an "expert must have 'good grounds' for his or her belief"); *In re TMI Litig.*, 193 F.3d 613, 697 (3d Cir. 1999) (holding, "If the data underlying the expert's opinion are so unreliable that

no reasonable expert could base an opinion on them, the opinion resting on that data must be excluded.”).

To illustrate, in Paragraphs 141 and 190 of his report, which present the overarching core of Dr. Afnan’s opinions regarding ZHP’s compliance with cGMPs and other regulatory obligations, and with regard to the July 27, 2017 smoking gun email, he explicitly relies on Dr. Xue and states:

As explained in detail in the report of Fengtian Xue, ZHP’s scientists did not have a reasonable scientific basis to expect that NDMA or NDEA could form during either the TEA with quenching or Zinc Chloride processes; thus, ZHP did not have a reason to investigate nitrosamines at the time the company was performing its risk assessments for these processes. (*See* Xue Rep. at Section V.B.2.)

* * *

But as detailed in the report of Fengtian Xue, an expert chemist with native fluency in Chinese, Plaintiffs’ experts misread this highly technical email. (*See* Xue Rep. at Section VI.) As Dr. Xue explains, the [July 27, 2017] email does not establish ZHP’s awareness of a potential for the formation of NDMA or NDEA as a result of the valsartan API production processes, but instead addresses the potential for entirely different impurities in different drug substances. (*Id.*)

(Ex. 1). The subheadings of the surrounding parts of Dr. Afnan’s report illustrate how these two paragraphs underpin the rest of his opinions concerning ZHP’s compliance with cGMPs and other regulatory requirements:

A. ZHP Conducted And Disclosed Appropriate Risk
Analyses Of The Zinc Chloride And TEA With

Quenching Processes Consistent With CGMPs And Regulatory Requirements.

B. ZHP Performed Appropriate Testing Pursuant To Regulatory Requirements And CGMPs While Valsartan Was On The Market.

C. ZHP Properly Responded To Identification Of Trace Amounts Of Nitrosamines In Valsartan API.

D. ZHP's API Was Not Adulterated.

(Ex. 1, at p. i). The following specific statements are emblematic of Dr. Afnan's reliance on Dr. Xue's chemistry opinions:

- “***First***, ZHP conducted appropriate risk assessments of each of the relevant changes to the API manufacturing process (TEA with quenching and Zinc Chloride) based on what was known at the time those manufacturing changes were made. ZHP also disclosed the content and results of those assessments to the FDA for review and approval through the ANDA process. To the contrary, after nitrosamines were identified in valsartan API in May 2018, the FDA repeatedly stated that ***neither industry nor regulators were aware*** that NDMA or NDEA could form during the manufacture of valsartan API prior to May 2018” (*Id.* at ¶ 135). **This opinion relies on both Dr. Xue's excluded opinions.**
- “Plaintiffs' experts presented any evidence that, prior to May 2018, ZHP knew of the potential for nitrosamine impurities in valsartan API such that it would have had reason to go beyond industry testing standards and use GC-MS testing to identify unknown impurities below 0.10%.” (*Id.* at ¶ 136). **This opinion is clearly contradicted by the July 27, 2017 email without Dr. Xue's reimagining to rely on.**
- “***Third***, ZHP responded appropriately to the discovery of nitrosamines in valsartan API in May 2018, including by enacting a voluntary recall and withdrawing all valsartan API from the United States market.” (*Id.* at ¶ 137). **Same as prior example.**
- “ZHP performed lengthy, thorough investigations of these processes before

submitting the manufacturing changes to the FDA to analyze potential risks, including an investigation of the potential for impurities.” (*Id.* at ¶ 139). **Dr. Afnan’s only concrete, non-conclusory basis for this opinion is Dr. Xue’s now excluded chemistry opinions, including what was knowable.**

- “But ZHP concedes that the company did not specifically investigate the potential for nitrosamines in its API prior to May 2018. As detailed throughout this report, this does not constitute a CGMP violation because neither ZHP, nor manufacturers of finished dose valsartan products, nor the FDA had a reasonable scientific basis to suspect that nitrosamines could form as a result of ZHP’s manufacturing processes.” (*Id.* at ¶ 160). **Again, this opinion relies directly on Dr. Xue’s excluded opinion as to what was knowable, and is clearly contradicted by the July 27, 2017 email without Dr. Xue’s reimagining to rely on.**
- “The realities of what was known at the time these processes were developed demonstrate that ZHP did not have a reasonable basis to test for nitrosamines in its API.” (*Id.* at ¶ 170). **Dr. Afnan’s only concrete, non-conclusory basis for this opinion is Dr. Xue’s now excluded chemistry opinions.**
- “Again, compliance with CGMPs turns on what is reasonably known at the time product manufacturing takes place – not information that becomes available after the manufacturing conduct has stopped.” (*Id.* at ¶ 171). **Same as the prior example.**
- “By contrast, as set forth above, there would have been no expectation that the processes used to synthesize valsartan API would generate trace amounts of dimethylamine, which could lead to formation of NDMA via secondary reaction under special circumstances (in the presence of nitrous acid). (*Id.* at 234.) After all, there had been no literature indicating that NDMA was a potential impurity in valsartan API prior to June 2018. (*Id.*)” (Ex. 1, at ¶ 176). **Same as the prior example.**
- “Reasonably expected impurities would not include NDMA or NDEA because, as discussed above....” (*Id.* at ¶ 181). **Same as the prior example.**
- “ZHP also promptly and properly reported its finding of NDMA/NDEA in valsartan API and took appropriate action consistent with FDA regulations and relevant guidance documents.” (*Id.* at ¶ 188). **Again, this opinion is**

clearly contradicted by the July 27, 2017 email without Dr. Xue's reimagining to rely on.

- “ZHP was put on notice that there was something to investigate with respect to nitrosamines in valsartan API for the first time in May 2018.” (*Id.* at ¶ 191). **This opinion relies on both of Dr. Xue's excluded opinions.**
- “To the extent they address the recall, it is only to suggest that it should have happened earlier. (*E.g.*, Plunkett Rep. at 32-33.) This suggestion is based on the presumption that NDMA/NDEA impurities should have been discovered earlier, which is incorrect for all of the reasons disussed [(sic)] above.” (*Id.* at ¶ 193). **Dr. Afnan's only concrete, non-conclusory basis for this opinion is Dr. Xue's now excluded chemistry opinions.**
- “But the reference in the Form 483 to the ‘potential impact’ of the process change is obviously a reference to the production of NDMA and NDEA impurities (the possibility of which was first discovered in May 2018), not an abstract concern of the FDA about the change or the formality of ZHP's risk assessments.” (*Id.* at ¶ 201). **Again, this opinion is clearly contradicted by the July 27, 2017 email without Dr. Xue's reimagining to rely on.**
- “Moreover, at the end of the same month in which the FDA issued the Form 483, it told the public that ‘neither regulators nor industry fully understood how NDMA could form during this process,’ and they were ‘still not 100 percent sure that this is the root cause of the problem’ at that time.” (*Id.* at ¶ 202). **This relies on both the major opinions relying on Dr. Xue, and the July 27, 2017 email was never produced to or addressed by the FDA, and it contradicts Dr. Afnan's ability to rely on this statement from the FDA, as it explicitly identified NDMA in valsartan as well as its root cause.**
- “Third, the FDA's CGMP observations were made in hindsight, in an effort to determine how the nitrosamine contamination eluded so many scientists and regulators. Newer information not available while a product was on the market cannot retroactively render a product adulterated.” (*Id.* at ¶ 210). **This opinion relies on both Dr. Xue's excluded opinions.**

Dr. Afnan also provides extensive commentary on Dr. Hecht's chemistry opinions, which he could only do by relying on Dr. Xue's now excluded chemistry opinions.

(*Id.* at ¶ 139-140, 146, 171-172, 185). Dr. Afnan does the same thing with respect to Dr. Najafi's chemistry opinions. (*Id.* at ¶ 139-140, 145-146, 150, 171-172, 184-185, 198, 200-202). Thus, Dr. Afnan's opinions claiming ZHP complied with cGMPs and other regulatory requirements are unsupported without reliance on Dr. Xue's now excluded opinions.

During his deposition, Dr. Afnan conceded his extensive reliance on Dr. Xue to answer the organic chemistry question of whether the reactions at issue could have been identified as possibilities and related issues. (Afnan 3/8/2023 Dep. Tr. 156:6-11, 157:2-13, 171:3-5, 205:19-206:4, 206:9-15, 213:17-20, 230:20-231:6, 410:23-411:2). Defense counsel confirmed this. (*Id.* at 175:22-176:5). Without Dr. Xue's opinions to rely on, Dr. Afnan cannot opine on whether ZHP performed a proper risk assessment for the ZnCl₂ or TEA with sodium nitrite quenching processes in accordance with cGMPs or other regulatory requirements (the FDA of course found that ZHP did not). He also cannot opine that ZHP continued to comply with cGMPs or other regulatory obligations after ZHP gained the knowledge documented in the July 27, 2017 email. The Court should consequently exclude Paragraphs 134-212 of his report, captioned "ZHP Complied with Regulatory Requirements in the Manufacture and Sale of Valsartan API," as well as any paragraphs containing those opinions.⁴

⁴ Plaintiffs note that the Court excluded Dr. Bain (Dr. Afnan's true counterpart) in

Looking forward, the ZHP Defendants cannot now claim Dr. Afnan has the necessary expertise to proffer his own chemistry opinions without Dr. Xue to rely on. Dr. Afnan testified in his deposition that he is an expert in cGMPs, **not** an expert in the fields of organic chemistry or toxicology. (Afnan 3/8/2023 Dep. Tr. 63:8-11, 63:17-64:2). Later in his deposition, after Dr. Afnan tried to re-open the door so that he could give chemistry opinions, he backtracked and confirmed that Dr. Xue was addressing the chemistry: **“I did not say that I was giving chemistry opinions...My expertise in this is GMPs...My role, my remit, was to look at the plaintiff experts and assess GMP – GMP statements. I was not here, on this project, to assess the chemistry. For that, there was Professor Xue.”** ZHP’s counsel confirmed that Dr. Afnan was not proffered as an expert in chemistry, in objecting to a chemistry question, “Objection. That’s outside the scope of his opinions.” (*Id.* at 158:3-13, 168:11-171:11). To further illustrate, when asked whether he evaluated “what temperatures were reached and what impact that could have on the DMF,” during the zinc chloride process, he replied, **“Again, my remit here was not chemistry.”** (*Id.* at 173:11-16). Thus, since Dr. Xue’s opinions on that and the other points has been precluded, any opinion relying on or discussing the chemistry issues must also be precluded.

The same goes for Dr. Afnan’s reliance on Dr. Xue’s excluded opinions

this manner. ([ECF 2581](#), p. 18-19).

regarding the July 27, 2017 email. In addition to stating his reliance in his report, quoted above, in his deposition Dr. Afnan confirmed his reliance on Dr. Xue's opinion as to what the email said and meant, as the foundation for his opinions as to the lack of significance of that email. (*Id.* at 206:9-15). Dr. Xue's opinion has been precluded; thus, Dr. Afnan cannot rely on it.

Finally, to the extent that Defendants may assert that Dr. Afnan claims that he relied on an off the record discussion that ZHP witness Jucai Ge had with ZHP employee Jinsheng Lin, in an effort to undercut the import of the July 27, 2017 email authored by Dr. Lin, this should be also precluded. Simply put, Jucai Ge's deposition testimony was based on her conversation with Jinsheng Lin, which renders it inadmissible hearsay if presented affirmatively. (Jucai Ge 5/26/2022 Dep. Tr. 79:7-16 (Ex. 11))). *See Chevron TCI, Inc. v. Capitol House Hotel Manager, LLC*, 541 F. Supp. 3d 687, 694 (M.D. La. 2021) (holding that "a corporate representative may not testify to matters outside his own personal knowledge 'to the extent that information [is] hearsay not falling within one of the authorized exceptions.'") (quoting *Brazos River Auth. v. GE Ionics, Inc.*, 469 F.3d 416, 435 (5th Cir. 2006)) (citing *Deutsche Shell Tanker Gesellschaft mbH v. Placid Refining Co.*, 993 F.2d 466, 473 n. 29 (5th Cir. 1993)); *Diamond Offshore Co. v. Survival Sys. Int'l, Inc.*, 902 F. Supp. 2d 912, 932 (S.D. Tex. 2012) (holding: "The statements made on information and belief based on Mark Beatty's conversations with Captain Beatty

are hearsay and cannot be transformed into admissible evidence simply because Mark Beatty is a corporate representative.”).

Moreover, beyond the black letter inadmissibility of the hearsay testimony, Jucai Ge’s ipse dixit description of the email without specifying what it actually says is as unreliable as Dr. Xue’s attempt to proffer the same opinion—since she admitted that the email says what it clearly says. (Jucai Ge 5/26/2022 Dep. Tr. 83:7-84:7 (testifying that the email was “poorly written and complicated ... even though that was the words that said so on this page,” meaning Plaintiffs’ understanding of what the email actually states is accurate). Moreover, the only translation of the email produced by the ZHP Defendants confirms the statements relevant to Plaintiffs’ claims. (Ex. 12). And Dr. Afnan’s opinion is not helpful, at most repeating that her analysis characterized the email as “confusing” and “badly written.” (Afnan 3/8/2023 Dep. Tr. 215:4-7).

Dr. Afnan cannot rely on either person to support his decision to ignore the July 27, 2017 email. *Paoli*, 35 F.3d at 742-43; *TMI Litig.*, 193 F.3d at 697; *Gopalratnam*, 877 F.3d at 789; *Sims*, 839 F.3d at 405; *Fuesting.*, 362 F. App’x at 564. Thus, Dr. Afnan should be precluded from relying on the ex parte interviews, and any opinions based on those interviews should be precluded.

Moreover, when confronted with the clear language of the July 27, 2017 email, **Dr. Afnan attempted to sideline the email by inexplicably asserting that**

the NDMA was not formed as a result of the sodium nitrite quenching during the manufacturing process. (Afnan 3/8/2023 Dep. Tr. 230:5-18). Of course, the formation of the NDMA as a result of the sodium nitrite quenching process is not debatable, and was established by and admitted to by ZHP's corporate representatives, including Dr. Li. (Min Li 4/20/2021 Dep. Tr. 96:12-16 (Ex. 13);⁵ PRINSTON00075810-11, 75854 (Ex. 14); PRINSTON00076102-03 (Ex. 15)). Dr. Afnan then withdrew further and stated that he could not say when or how the NDMA was formed. (Afnan 3/8/2023 Dep. Tr. 230:20-231:6). He cannot provide a reliable opinion as to the implications of the formation of the NDMA without a reliable basis for understanding how the NDMA was formed. This is basic.

The complete absence of a reliable methodology was illustrated when Dr. Afnan was asked to assume that the July 2017 email says there was NDMA in valsartan and that it was formed due to the sodium nitrite quenching. He inexplicably still would not agree that would mean ZHP knew about those facts at least as of July 2017. (*Id.* at 234:15-235:2). Then, when asked whether, if ZHP knew about the potential formation of the nitrosamines but failed to test for their potential presence, that would be a cGMP violation, he could not or would not answer. (*Id.* at 235:19-236:7). A methodology that leads to any answer but "Yes"

⁵ Min Li also confirmed the content of the July 27, 2017 email. (*Id.* at 82:11-12, 87:19-88:7, 88:13-89:18).

to those questions is so flawed and so result-oriented that preclusion is required.

CONCLUSION

For the foregoing reasons, the Court should deny the ZHP Defendants' motion and grant Plaintiffs' cross-motion to exclude Dr. Afnan's opinions regarding ZHP's compliance with cGMPs and other regulatory requirements, all of which spring from his reliance on Dr. Xue now excluded opinions.

Dated: February 6, 2024

Respectfully submitted,

/s/ Ruben Honik

Ruben Honik

HONIK LLC

1515 Market Street, Suite 1100

Philadelphia, PA 19102

Phone: (267) 435-1300

ruben@honiklaw.com

/s/ Daniel Nigh

Daniel Nigh

**Nigh Goldenberg Raso & Vaughn,
PLLC**

14 Ridge Square NW

Third Floor

Washington, D.C. 20016

Phone: (850) 600-8090

dnigh@nighgoldenberg.com

/s/ Adam Slater

Adam Slater

**MAZIE, SLATER, KATZ &
FREEMAN, LLC**

103 Eisenhower Pkwy, 2nd Flr.

Roseland, NJ 07068

Phone: (973) 228-9898

aslater@mazieslater.com

/s/ Conlee S. Whiteley

Conlee S. Whiteley

KANNER & WHITELEY, LLC

701 Camp Street

New Orleans, LA 70130

Phone: (504)-524-5777

c.whiteley@kanner-law.com

MDL Plaintiffs' Co-Lead Counsel

/s/ Jorge Mestre

Jorge Mestre

RIVERO MESTRE LLP

2525 Ponce de Leon Blvd., Suite 1000

Miami, FL 33134

Phone (305) 445-2500

jmestre@riveromestre.com

/s/ Gregory P. Hansel

Gregory P. Hansel

**PRETI, FLAHERTY, BELIVEAU &
PACHIOS, CHARTERED, LLP**

One City Center

P.O. Box 9546

Portland, ME 04112

Phone: (207) 791-3000

ghansel@preti.com

***Third-Party Payor Economic
Loss Co-Lead Class Counsel***